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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,517	03/16/2004	Xiaoyang Qi	10872.0529639	4062

26874 7590 11/16/2006

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/801,517	QI, XIAOYANG	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *9-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 44-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Qi

1. Applicant's response filed on 10/3/2006 is acknowledged. Claims 1-57 are pending. Claims 9-43 are withdrawn from further consideration as being drawn to non-elected inventions. Claims 1-8 and 44-49 are amended. New claims 50-57 are added.

2. Claims 1-8 and 44-57 are under examination are under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections Withdrawn

4. The objections to the specification because it contains an embedded hyperlink and/or other form of browser-executable code is withdrawn in view of applicants' amendment to the specification.

5. The objection of claim 5 because it depends on itself is withdrawn in view of applicant's amendment to the claim.

Rejections Withdrawn

6. The rejection of claims 1-8 and 44-49 under 35 U.S.C. 102(b) as being anticipated by Morimoto et al. (J. Bio. Chem., 1990, 265(4): 1933-1937), and as evidenced by Morimoto et al. (Proc. Natl. Acad. Sci. U.S.A., 1989: 86: 3389-3393) is withdrawn in view of applicant's amendment to the claims.

7. The rejection of claims 1-8 and 44-49 under 35 U.S.C. 103(a) as being unpatentable over Vaccaro et al. (FEBS 1993, 336(1): 159-162) in view of the teachings of O'brien et al. (WO9503821A1) is withdrawn in view of applicant's amendment to the claims and new grounds of rejections.

Response to Arguments

8. The rejection of claims 1-8 and new claims 50-57 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

The response states that claims have been amended to limit the inner leaflet component to a phospholipids selected from the group consisting of phosphatidylserine, phosphatidylethanolamine, and structural analogs thereof. The response states that applicants have provided sufficient detailed examples in the specification showing peptides comprising less than the full amino acid protein depicted in SEQ ID NO:l and 2. The U.S. Patent Office clearly does not require a description of every embodiment for peptide claims and that while protein chemistry taken as a whole may be unpredictable, particular embodiments are patentable. Applicants have provided sufficient detail of particular patentable embodiments. Because of the unpredictability of living processes, generic biological claims inherently must cover inoperative members of the class. This is not fatal to the claim if a person skilled in the art can recognize which species are operative and which are not, especially if functional limitations are used to exclude inoperative members. In the present case, inoperative members

are specifically excluded through the functional limitations that the polypeptide must retain plasma-membrane affinity.

Applicant's arguments have been carefully considered but are not found persuasive. The amendment to the claims cannot overcome the instant rejection. While claims 1-8 have been amended to limit the inner leaflet component to a phospholipids selected from the group consisting of phosphatidylserine, phosphatidylethanolamine, and structural analogs thereof, claims 1-8 still recite a prosaposin-related polypeptide comprising an amino acid sequence substantially identical to and having 80% sequence identity to SEQ ID NO. 1 or 2. Furthermore, new claims 50-57 recite "a prosaposin-related polypeptide", which encompass polypeptides that are at least 80% identity to the amino acid sequence set forth in SEQ ID NO.I and fragments thereof (see specification page 4). As stated in the previous office action, the instant specification fails to provide sufficient descriptive information such as a core structure that is required for the function (i.e. retain plasma membrane affinity) and is common to the genus of the sequences that are at least 80% identical to SEQ ID NO.1 or 2 and fragments thereof. Therefore, applicants are claiming a genus of homologs and fragments that are only characterized by their functional characteristics i.e. retain plasma membrane affinity. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product,

or any combination thereof. In this case, the only factors present in the claim are recitation of "80% sequence identity", "a prosapsin-related polypeptide" and retains plasma membrane affinity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics such as a core structure that is required for the function, i.e. retain plasma membrane affinity, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and *Enzo Biochem, Inc. v. Gen-Probe Inc.* are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in *University Of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The Court stated that" [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. at 1567, 43 USPQ2d at 1405. The court also stated that:

> *a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can*

> *do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.*

Id. at 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See *Enzo Biochem, Inc. V. Gen-Probe Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The *Enzo* court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics .... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Id.* at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in *Lilly* and *Enzo* were DNA constructs *per se*, the holdings of those cases are also applicable to claims such as those at issue here. Thus the instant specification may provide an adequate written description of a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, or a prosaposin-related polypeptide, per *Lilly*, by structurally describing representative homologs or fragment by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per *Enzo*, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, and a prosaposin-related polypeptide useful in the claimed invention in a manner that satisfies either the *Lilly* or *Enzo* standards. Although the specification discloses SEQ ID NOs.1 and 2, it is broadly described and this does not provide a description of the broadly claimed homologues and fragments of SEQ ID NO.1 or 2, and a prosaposin-related polypeptide that would satisfy the standard set out in Enzo because the specification provides no functional characteristics coupled to structural features.

Further, the specification also fails to describe a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, and a prosaposin-related polypeptide by the test set out in *Lilly* because the specification describes only SEQ ID NO. 1 and 2 (i.e. full length).

Therefore it necessarily fails to describe a representative number of such species. Thus the specification does not provide an adequate written description of a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, and a prosaposin-related polypeptide that is required to practice the claimed invention.

9. The rejection of claims 1-8 and new claims 50-57 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent comprising an anionic phospholipid, particularly phosphatidylserine and a prosaposin polypeptide of SEQ ID NO.1 or SEQ ID NO.2, does not reasonably provide enablement for an agent comprising any and all inner leaflet component, and any and all prosaposin-related polypeptide of an amino acid sequence that is at least 80% identical to SEQ ID NO.1 or 2 is maintained.

The response states that applicants contend that the claims, as now amended, are fully enabled for the same reasons set forth in the response to written description rejection.

Applicant's arguments have been carefully considered but are not found persuasive. Because applicant fails to provide adequate written description for a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, and a prosaposin-related polypeptide for the reasons set forth above, one skilled in the art would not know how to identify the species encompassed by the claimed genus of polypeptide, as such one would not know how to make the broad class of a polypeptide that is at least 80% identical to SEQ ID NO. 1 or 2, and a prosaposin-related polypeptide that possess the

required function i.e. retain plasma-membrane affinity. Therefore, the rejection is proper and maintained.

10. The rejection of claims 1-3, 44-47 and new claims 50-52 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 16, 17, 21 and 22 of U.S. Patent No. 6,872,406 in view of Vaccaro et al. (FEBS Lett. 1994, 349: 181-186, IDS) is maintained.

Because applicant failed to respond to the rejection, the rejection is maintained.

11. The provisional rejection of claims 1-3, 44-47 and new claims 50-52 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 17, 21 and 22 of copending Application No. 10/967,921 in view of Vaccaro et al. (FEBS Lett. 1994, 349: 181-186, IDS) is maintained.

The response states that they will file a TD assuring that the present application and copending Application no. 10/967,921 will expire at the same time if conflicting claims are issued.

Because no TD has been filed, the rejection is maintained.

New Grounds of Rejections

12. Claims 1-8, 44-49 and new claims 50-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaccaro et al. (FEBS 1993, 336(1): 159-162) in view of the

teachings of O'brien et al. (WO9503821A1), as evidenced by Vaccaro et al. (FEBS, 1994, 349: 181-186, IDS) is maintained.

The teachings of Vaccaro (1993) and O'brien have been set forth in the previous office action.

The response states that Vaccaro et al. in view of O'brien et al. do not teach that the prosaposin-related polypeptide and the inner leaflet component form a nanovesicle. In such nanovesicles, the polypeptide is embedded within the lipid membrane by dynamic processes of saposin interactions with phospholipids membrane.

Applicant's arguments have been carefully considered but are not persuasive. The phosphatidylserine which were used by Vaccaro (1993) et al. in their assays is small unilamellar vesicles (SUV) or large unilamellar vesicles (LUV), wherein SUV were obtained by submitting the lipid suspension to sonication under nitrogen in a Branson B 15 Sonifier, and LUV were prepared by filter exclusion through two stacked 0.1 μm pore size polycarbonate filters using a high pressure extrusion apparatus (see page 160, left column section 2.7). Both SUV and LUV are nanovesicles. When such phosphatidylserine SUV or LUV were mixed with saposin C, they would have formed nanovesicles as evidenced by Vaccaro (1994) et al. Vaccaro (1994) et al. teach that the association (or binding) of Sap C and PS bilayers are spontaneous (see page 184, left column, lines 4-5, page 181, right column, 3rd paragraph). Furthermore, the sequence of saposin C taught by O'brien et al. is 100% identical to the instant SEQ ID NO.2 regardless of what sequence comparison program is used. Moreover, the sequence comparison program Blosum 67 used by STIC is equivalent to the GCG

program GAP. Therefore, Vaccaro (1993) in view of O'brien teach every limitation of the claims.

Claim Rejections - 35 USC § 112, 2nd paragraph

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 2, 5, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 2 recites the limitation "the biocompatible phospholipid" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

B. Claim 5 recites the limitation "fusogenic polypeptide" in claim 2. There is insufficient antecedent basis for this limitation in the claim.

C. Claim 7 recites the limitation "the biologically active portion of prosaposin polypeptide" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

15. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit: 1643
Nov. 5, 2006

CHRISTOPHER H. YAEN
PRIMARY EXAMINER